

Joukov, Vladimir

SEQUENCE LISTING

<120> VASCULAR ENDOTHELIAL GROWTH FACTOR C (VEGF-C) PROTEIN
AND GENE, MUTANTS THEREOF, AND USES THEREOF

<130> 28967/34140A

<140> US 09/534,376

<141: 2000-03-24

<150: 09/355,700

-:151:- 1999-11-05

:150: PCT/US98/01973

-:151: 1998-02-02

<150: 08/795,430

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::150: PCT/FI96/00427

<151> 1996-08-01

<:150 08/671,573</pre>

:151 - 1995-06-28

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:151 - 1996 -02-14

:150 08/585,895

4:151 - 1995-01-12

<150 - 08/510,133

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:150: 08/340,011

:151/ 1994-11-14

:160 - 59

:170 - PatentIn Ver. 2.0

:210 - 1

-:211 - 4416

:212 DNA

4213 / Homo sapiens

:220 -

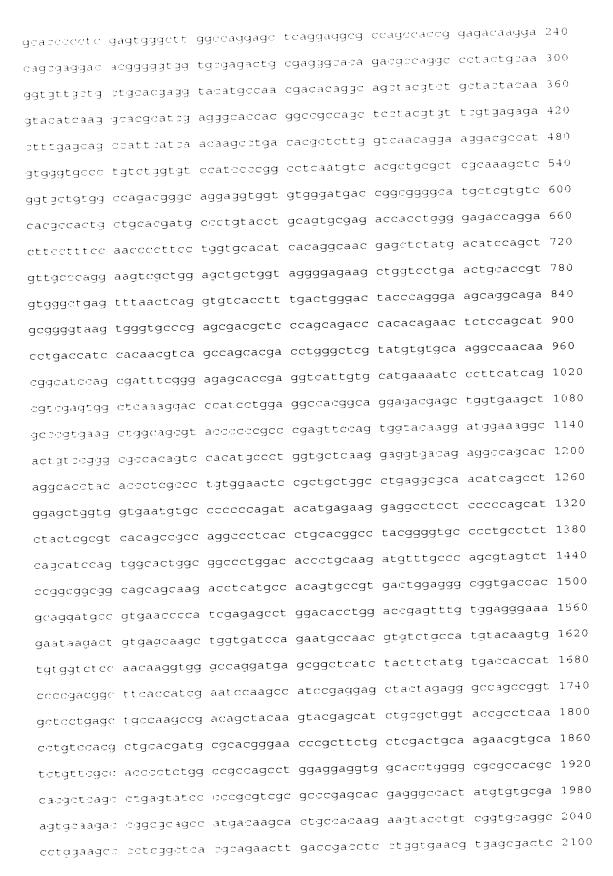
:223 - Human Flt4 cDNA (short form)

:220 -

:223 - At position 4243, n=A,T,G or C

:400 - 1

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getggagatg cagtgettgg tygeeggage geaegegeee ageategtgt ggtacaaaga 2160 egagaggety etggaggaaa agtetggagt egaettggeg gaeteeaace agaagetgag 2220 datedagege gtigegegagg aggatigegig aegetatetig tigeagegtigt geaaegeeaa 2280 gggotgogt: aactootoog obagogtggo ogtggaaggo toogaggata agggbagdat 2340 ggagatogty atoettgtog gtacoggogt categotyte ttottetggg toetestoct 2400 octoatotto tytaacatga gyaggooggo ocaogoagab atcaagacgy gotacotyto 2460 datdatdaty gaddoogggg aggtgddtot ggaggagdaa tgdgaatadd tgtddtadga 2520 tgccagccay tgggaattee ecegagageg getgcacetg gggagagtge teggetaegg 2580 ogosttoggg aaggtggtgg aagestoogs titoggsats cacaagggsa gcagstgtga 2640 caccytygec ytyaaaatyc tyaaayayyy cyccacyycc aycyaycacc ycycyctyat 2700 gtoggagoto aagatootoa ticacatogg caaccacoto aacgiggica accidetegg 2760 ggcgtgcacc aagccgcagg gccccctcat ggtgatcgtg gagttctgca agtacggcaa 2820 octotocaac ttootgogog ocaagoggga ogcottoago ocotgogogg agaagtotoo 2880 egageagege ggaegettee gegeeatggt ggagetegee aggetggate ggaggeggee 2940 ggggagcage gacagggtee tettegegeg gttetegaag acegagggeg gagegaggeg 3000 ggottotoca gascaagaag otgaggacot gtggotgago oogotgacca tggaagatot 3060 tgtotgotas agettocagg tggccagagg gatggagtto otggcttoco gaaagtgcat 3120 ccacagagae etggetgete ggaacattet getgteggaa agegaegtgg tgaagatetg 3180 tgactttggc cttgcccggg acatctacaa agaccctgac tacgtccgca agggcagtgc 3240 ccggctgccc ctgaagtgga tggcccctga aagcatcttc gacaaggtgt acaccacgca 3300 gagtgaegtg tggteetttg gggtgettet etgggagate ttetetetgg gggeeteese 3360 gtaccctggg gtgcagatca atgaggagtt ctgccagcgg ctgagagacg gcacaaggat 3420 gagggccccg gagctggcca ctcccgccat acgccgcatc atgctgaact gctggtccgg 3480 agaccccaag gegagacetg cattetegga getggtggag ateetggggg acetgeteea 3540 gggcaggggc ctgcaagagg aagaggaggt ctgcatggcc ccgcgcagct ctcagagctc 3600 agaagaggge agettetege aggtgteeae catggeeeta cacategeee aggetgaege 3660 tgaggadago dogodaagoo tgdagogoda dagootggoo godaggtatt adaactgggt 3720 gteettteee gggtgeetgg ceagagggge tgagaeeegt ggtteeteea ggatgaagae 3780 atttgaggaa tteeccatga eeccaaegae etacaaagge tetgtggaca accagacaga 3840 cagtgggatg gtgctggcct cggaggagtt tgagcagata gagagcaggc atagacaaga 3900 aageggette aggtagetga ageagagaga gagaaggeag cataegteag cattttette 3960 totgoactta taagaaagat caaagacttt aagactttog otatttotto taotgotato 4020 tactacaaac ttcaaagagg aaccaggagg acaagaggag catgaaagtg gacaaggag 4080 gtgaccactg aagcaccaca gggaaggggt taggcctccg gatgactgcg ggcaggcctg 4140 gataatatec agcctccaa aagaagctgg tggagcagag tgttccctaa ctcctccaag 4200 gaaaggggaga ccaaagaggaga ccaaagaggaga ccaaagaggaga ccaaagaggaga ccaaagaggaga ccaaagaggaga ccctttcaagaggagaga ccaaagaggaga cccttatgcca gcgtgacaga gggctcacct 4320 cttgccttct aggtcactt tcacacaaatg tcccttcaga acctgaccat gtgcccgcca 4380 gttattcctt ggtaatatga gtaatacatc aaagagg

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tacaacagcg agtatggga gctgtcggag ccaagcgagg aggaccactg ctccccgtct 180
gcccgcgtga ctttcttcac agacaacagc tactaa
215

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His Arg Gln Glu Ser Gly Phe Arg
          35
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 <211> 18
 <212> PRT
 <213> Homo sapiens
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 <223> At position 1, Xaa = Unknown
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   1
  Leu Lys
  3211> 219
  -212> DNA
  <213> Artificial Sequence
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         human VEGF-C cDNA
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   gtggtggaat tcgacgaact catgactgta ctctacccag aatattggaa aatgtacaag 120
   tgtcagctaa ggcaaggagg ctggcaacat aacagagaac aggccaacct caactcaagg 180
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165

ago tao oto ago aag aog tia tit gaa att ada gig oot oto tot daa - 933 Ser Tyr Leu Ser Lys Thr Leu Phe Glu lle Thr Val Pro Leu Ser Gln 180 - 185	
ggc ccc aaa cca gta aca atc agt ttt gcc aat cac act tec tgc cga 981 Gly Pro Lys Pro Val Thr lle Ser Phe Ala Asn His Thr Ser Cys Arg 200 200	
tgc atg tct aaa ctg gat gtt tac aga caa gtt cat tcc att att aga 102 tgc atg tct aaa ctg gat gtt tac aga caa gtt cat tcc att att aga 102 Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg 225 220	19
cgt tcc ctg cca gca aca cta cca cag tgt cag gca qcg aac aag acc 10° Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn Lys Thr 230 235	77
tgc ccc acc aat tac atg tgg aat aat cac atc tgc aga tgc ctg gct 11 Cys Pro Thr Asn Tyr Met Trp Asn Asn His Ile Cys Arg Cys Leu Ala	25
cag gaa gat ttt atg ttt tcc tcg gat gct gga gat gat edd abb S Gln Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser Thr Asp 270	.73
gga ttc cat gac atc tgt gga cca aac aag gag ctg gat gaa gag acc 12 gga ttc cat gac atc tgt gga cca aac aag gag ctg gat gaa gag acc 12 Gly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu Glu Thr 280 280 285	221
7/5	269
cac aaa gaa cta gac aga aac tca tgc cag tgt gtc tgt aaa aac aaa 1 His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys Asn Lys 315	317
ctc ttc ccc agc caa tgt ggg gcc aac cga gaa ttt gat gad add dom Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu Asn Thr	365
tgc cag tgt gta tgt aaa aga acc tgc ccc aga aat caa ccc ccd dar Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro Leu Asn 350	1413
cct gga aaa tgt gcc tgt gaa tgt aca gaa agt cca cag aaa tgc bos Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys Cys Leu 365	1461
tta aaa gga aag aag ttc cac cac caa aca tgc agc tgt tac aga cgg tta bys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr Arg Arg Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr Arg Arg 385	1509
cca tgt acg aac cgc cag aag gct tgt gag cca gga ttt tca tat agt Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser Tyr Ser 390 395	1557
gaa gaa gtg tgt cgt tgt gtc cct tca tat tgg aaa aga cca caa atg Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro Gln Met 415	1605
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د210× 8

d211: 419

:212: PRT

<213> Homo sapiens

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Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu Ala 35 40

Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser 50 55 60

Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys Met 65 70 75 80

Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu Gln
85
90
95

Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala 100 105

His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys 115 120 125

Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe 130 135

Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val Tyr 145 150 150

Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr \$165\$

Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu 180 185 190

Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser

Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile 210 215 lle Arg Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn 225 Lys The Cys Pro The Ash Tyr Met Trp Ash Ash His Ile Cys Arg Cys Leu Ala Gln Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser 265 Thr Asp 3ly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu Glu Thr Cys Gln Cys Val Cys Arg Ala Gly Leu Arg Pro Ala Ser Cys Gly Pro His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys 310 Asn Lys Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu 330 Asn Thr Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro Leu Asn Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys Cys Leu Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr Arg Arg Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser Tyr Ser Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro 410 405 Gln Met Ser <210: 9 .011: 17 -212 PRT :213 - Artificial Sequence <223 Description of Artificial Sequence: peptide %223 > VEGF-C peptide "PAM126" Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile Leu Lys < 210: 10 -211: 1836 +:212> DNA Registration 2013 - Murine

- 11 -

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cotgogodag coaacggaco ggootoootg otoocggtoo atocaco atg cac ttg 176 Met His Leu 1
ctg tgc ttc ttg tct ctg gcg tgt tcc ctg ctc gcc gc
ccc agt ccg cgc gag gcg ccc gcc acc gtc gcc gcc ttc gag tcg gga 272 Pro Ser Pro Arg Glu Ala Pro Ala Thr Val Ala Ala Phe Glu Ser Gly 20 25 30 35
ctg ggc ttc tcg gaa gcg gag ccc gac ggg ggc gag gtc aag gct ttt 320 Leu Gly Phe Ser Glu Ala Glu Pro Asp Gly Gly Glu Val Lys Ala Phe 40 45
gaa ggc aaa gac ctg gag gag cag ttg cgg tct gtg tcc agc gta gat 368 Glu Gly Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser Ser Val Asp 55 60
gag ctg atg tot gto otg tac oca gad tac tgg aaa atg tac aag tgc 416 Glu Leu Met Ser Val Leu Tyr Pro Asp Tyr Trp Lys Met Tyr Lys Cys 70 75
cag ctg cgg aaa ggc ggc tgg cag cag ccc acc ctc aat acc agg aca 464 Gln Leu Arg Lys Gly Gly Trp Gln Gln Pro Thr Leu Asn Thr Arg Thr 85
ggg gac agt gta aaa ttt gct gct gca cat tat aac aca gag atc ctg 512 Gly Asp Ser Val Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile Leu 100 115
aaa agt att gat aat gag tgg aga aag act caa tgc atg cca cgt gag 560 Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg Glu 120 125
gtg tgt ata gat gtg ggg aag gag ttt gga gca gcc aca aac acc ttc 608 Val Cys Ile Asp Val Gly Lys Glu Phe Gly Ala Ala Thr Asn Thr Phe 135
ttt aaa oot ooa tgt gtg too gto tao aga tgt ggg ggt tgo tgo aac - 656 Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys Asn 150 - 155
ago gag ggg otg oag tgo atg aac aco ago aca ggt tao oto ago aag 704 Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Gly Tyr Leu Ser Lys 165
acg ttg ttt gaa att aca gtg cct ctc tca caa ggc ccc aaa cca gtc 752 Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro Val 180 185

aca atc a Thr lle S	er Ph	e Ala 200	Asn .	HIS	1111	Ser '	205	nig	0,0			210		800
gat gtt t Asp Val T	ac ag Tyr Ar 21	g Gin	gtt Val	cat His	tca Ser	att 1le 220	att Ile	aga Arg	cgt Arg	tct Ser	ctg Leu 225	cca Pro	gca Ala	848
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gtg tgg a Val Trp 2 245	aat aa Asn As	c tac n Tyr	atg Met	tgc Cys 250	cga Arg	tgc Cys	ctg Leu	gct Ala	cag Gln 255	cag Gln	gat Asp	ttt Phe	atc Ile	944
ttt tat Phe Tyr 260	tca aa Ser As	at gtt sn Val	gaa Glu 265	gat Asp	gac Asp	tca Ser	acc Thr	aat Asn 270	gga Gly	ttc Phe	cat His	gat Asp	gtc Val 275	992
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tgt gga Cys Gly 325	gcc a Ala A	ac agg sn Arg	g gaa g Glu	ttt Phe	: Apl	gag Glu	aat Asr	aca n Thi	a tgt c Cys 335		g tgt n Cys	gta Val	a tgt L Cys	1184
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tgt gaa Cys Glu	tgt a Cys :	aca ga Thr Gl 36	u Ası	e aca n Thi	a cag r Gl:	g aaq n Lys	g tgo s Cy: 36		c ct e Le	t aa u Ly	a gge s Gl	g aa y Ly 37	g aag s Lys 0	1280
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ctg aag Leu Lys	g cat s His 390	tgt ga Cys As	at cc sp Pr	a gg o Gl	a ct y Le 39	u se	c tt r Ph	t ag e Se	jt ga er Gl	a ga u Gl 40	ia gt .u Va)0	a tg 1 Cy	c cgc s Arg	1376
tgt gto Cys Val 409	l Pro	tcg ta Ser Ty	at tg yr Tr	g aa p Ly 41	SAL	gg cc tg Pr	a ca o Hi	t ct s Le	eu As 41		agat	cata	ı	1422
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<213> Murine

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Lys Ala Phe Glu Gly Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser
50 60

Ser Val Asp Glu Leu Met Ser Val Leu Tyr Pro Asp Tyr Trp Lys Met 65 70 75 80

Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln Gin Pro Thr Leu Asn 85 90 95

Thr Arg Thr Gly Asp Ser Val Lys Phe Ala Ala Ala His Tyr Asn Thr 100 105 110

Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met 115 120 125

Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe Gly Ala Ala Thr 130 135

Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly 145 150 155 160

Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Gly Tyr 165 170 175

Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro 180 185 190

Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser Cys Arg Cys Met 195 200 205

Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg Ser 210 215

Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn Lys Thr Cys Pro 225 230 235 240

Thr Asn Tyr Val Trp Asn Asn Tyr Met Cys Arg Cys Leu Ala Gln Gln 255

Asp Phe Ile Phe Tyr Ser Asn Val Glu Asp Asp Ser Thr Asn Gly Phe 260 265

His Asp Val Cys Gly Pro Asn Lys Glu Leu Asp Glu Asp Thr Cys Gln 280 Cys Var Cys Lys Gly Gly Leu Arg Pro Ser Ser Cys Gly Pro His Lys Glu Leu Asp Arg Asp Ser Cys Gln Cys Val Cys Lys Asn Lys Leu Phe 3 (+5 Pro Asn Ser Cys Gly Ala Asn Arg Glu Phe Asp Glu Asn Thr Cys Gln 325 Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro Leu Asn Pro Gly 345 Lys Cys Ala Cys Glu Cys Thr Glu Asn Thr Gln Lys Cys Phe Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr Arg Arg Pro Cys Ala Asn Arg Leu Lys His Cys Asp Pro Gly Leu Ser Phe Ser Glu Glu 390 Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro His Leu Asn 410 210 ⇒ 13 +211: 1/41 +212: DNA 213: Quail . 220 3221 CDS :21:2 - (453) .. (1706) <220 · <223 - Quail VEGF-C cDNA generagong agogetenge gegnagenge egggenggge eggenegegg agggegeget 60 gegageggee actgggteet getteectee tteeteteee teeteeteet eeteettete 120 totgogottt ccacogotoc ogagogagog caogotogga tgtooggttt cotggtgggt 180 tttttacctg gcaaagtccg gataacttcg gtgagaattt gcaaagaggc tgggagctcc 240 cctacaageg tetgggaget getgeegeeg tegeatette teeateeege ggattttaet 300 geettgyata ttgcgagggg agggaggggg gtgaggacag caaaaagaaa ggggtggggg 360 gggqgagaga aaaggaaaag aaggageete ggaattgtge eegeatteet gegetgeeee 420 gegaceecce teegetetge cateteegea ca atg cae ttg etg gag atg ete Met His Leu Leu Glu Met Leu ted otg ggd tgd tgd dtd gdt gdt ggd gdd gtg dtd dtg gga ddd dgg 521 Ser Leu Gly Cys Cys Leu Ala Ala Gly Ala Val Leu Leu Gly Pro Arg 15 1.0

cag cc Gln Pr 2	g co o P 5	ad g no V	gto (Tal :	gec Ala	gcc Ala	gee Ala 30	tac Tyr	gaş	g to u Se	er C	igg Hy	cac His 35	ggc Gly	ta Ty	c ta r Tj	ad ⊊ Zr C	gag J u	569
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gaa ga Glu Gl	ag c lu G	ag (ln)	ttg Leu	cga Arg 60	tct Ser	gtg Val	tcc Ser	ag Se		tg 9 al 2 65	gat Asp	gaa Glu	ctc Lev	: at ∟M∈	ga et T	ca hr 70	gta Val	665
ctt ta Leu Ty	ac c yr F	dda (Pro	gaa Glu 75	tac Tyr	tgg Trp	aaa Lys	atg Met	_ E I	c a ne L 30	ıaa ∍y's	tgt Cys	cag Gln	tt: Le:	gaç ıAı	gg a rg L 85	iāa Jys	gga Gly	713
ggt to Gly T	gg (rp (caa 31n 90	cac His	aac Asn	agg Arg	gaa Glu	cac His	5 2.0	er S	agc Ser	tct Ser	gat Asp	aca Thi	a ag r A	ga t rg S	ca Ser	gat Asp	761
gat t Asp S 1	ca fer 1	ttg Leu	aaa Lys	ttt Phe	gcc Ala	gca Ala 110	HI	a ca a H	at † is '	tat Tyr	aat Asn	gca Ala 115		ga u I	tc (le 1	ctg Leu	aaa Lys	809
agt a Ser I 120	itt [le	gat Asp	act Thr	gaa Glu	tgg Trp 125) ALC	a aa g Ly	a a s T	cc hr	cag Gln	ggc Gly 130		g cc : Pr	a c o A	gt (gaa Glu	gtg Val 135	857
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gaa (Glu (Gly	Leu 170	Gli	n Cy	s Me	t. AS	1	75	361	1111	1.0	1	1	30				
	Phe 185	Glu	ı II	e Th	r va	191	90	eu	JCI	111	,	19	5	•				
gtc Val 200	Ser	Phe	e Al	a As	n H1	.s 11)5	11 3	CI	Cys	1123	21	. 0					21	5
gtt Val	tac Tyr	aga Ar	a ca g Gl	n va	it ca al Hi 20	at to is Se	ct a er I	tc	ata Ile	aga Are 22	J	gt to :g Se	ec t er I	tg .eu	cca Pro	gc A1 23	a ac a Th O	a 1145 r
caa Gln	act Thr	ca Gl	g tg n Cy 23	/s H	at g is V	eg g	ca a la <i>P</i>	aac Asn	aag Lys 240	, 111	c to r Cy	gt c ys P	ca a ro I	aa Jys	aat Asn 245	ca Hi	t gt s Va	ic 1193
Trp	Ası	n As 25	n G	!n i	tt t le C	λa y	irg (255	DC.				:	260				
tct Ser	to Se 26	r Hi	ac c Is L	tt g eu G	ga g ly A	sp s	ct o Ser . 270	gac Asp	aca Th	a to r Se	et g er G	aa g lu C 2	iga Sly 175	ttc Phe	cat Hi:	t at s []	it to le C	gt 1289 ys

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61 y 999	cct Pro	Asn	aaa Lys	gaa Glu	ttt Phe	gat Asp	gaa Glu 335	Olu	aag Lys	tgc Cys	cag Gln	tgt Cys 340	gta Val	tgt Cys	aaa Lys	1481
aag Lys	Thr	CAa		aaa Lys	cat His	cat His	5 PIC	cta Leu	aat Asn	cct Pro	gca Ala 355	aaa Lys	tgc Cys	ato ; Ile	tgc Cys	1529
gaa Glu 360	345 tgt Cys		a gaa c Glu	ı tct ı Ser	ccc Pro 365	aat Asi		tgt Cys	ttc Phe	tta Leu		gga Gly	aaa / Lys	a aga s Arg	ttt g Phe 375	1577
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gt <i>a</i> Val	cg Ar	c ac g Th 41	a tc ır Se	t ta	g aa p Ly	a ag s Ar	ja cc g Pr 41	Опс	t at u Me	g aa t As	t ta n	agcg	aaga	aag	cactac	t 1726
cgo	ctat		g tgt	cg												1741
420 420	10: 11:- 12> 13:-	418	i 1													
	1				5					_					la Gly 15	
Al	a Va	al L	eu L	eu G 20	ly Pi	ro A	rg G	ln Pi	ro P [.] 25	ro V	al A	la A	la A	la T	yr Glu	
Se	er G	ly H	is G 35	ly T	yr T	yr G	lu G	lu G 40	lu P	ro G	ly A	la G	ly G 45	lu P	ro Lys	
Αl		is A 50	la S	er L	ys A	sp L	eu G 55	lu G	lu G	ln L	eu A	rg S 60	er V	al S	er Ser	
			}lu L	eu M	1et T	hr \ 70	Jal I	eu T	yr P	ro G	lu T 75	yr T	rp I	ys M	let Phe 80	
		ys C	3ln I	∍eu A	Arg L	ys (Gly C	Gly T	rp G	ln F 90	lis A	Asn A	arg (Glu F	His Ser 95	Ē

Ser Ser Asp Thr Arg Ser Asp Asp Ser Leu Lys Phe Ala Ala Ala His 105 Tyr Asn Ala Glu Ile Leu Lys Ser Ile Asp Thr Glu Trp Arg Lys Thr Gln Gly Met Pro Arg Glu Val Cys Val Asp Leu Gly Lys Glu Phe Gly 135 Ala Thr Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Ile Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Ile Ser Thr Asn Tyr Ile Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser 185 130 His Gly Pro Lys Pro Val Thr Val Ser Phe Ala Asn His Thr Ser Cys 200 Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg Ser Leu Pro Ala Thr Gln Thr Gln Cys His Val Ala Asn Lys 235 230 225 Thr Cys Pro Lys Asn His Val Trp Asn Asn Gln [le Cys Arg Cys Leu Ala Gln His Asp Phe Gly Phe Ser Ser His Leu Gly Asp Ser Asp Thr 265 Ser Glu Gly Phe His Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu Glu Thr Cys Gln Cys Val Cys Lys Gly Gly Val Arg Pro Ile Ser Cys Gly Pro His Lys Glu Leu Asp Arg Ala Ser Cys Gln Cys Met Cys Lys Asn 310 Lys Leu Leu Pro Ser Ser Cys Gly Pro Asn Lys Glu Phe Asp Glu Glu 330 Lys Cys Gln Cys Val Cys Lys Lys Thr Cys Pro Lys His His Pro Leu Asn Pro Ala Lys Cys Ile Cys Glu Cys Thr Glu Ser Pro Asn Lys Cys Phe Leu Lys Gly Lys Arg Phe His His Gln Thr Cys Ser Cys Tyr Arg 375 Pro Pro Cys Thr Val Arg Thr Lys Arg Cys Asp Ala Gly Phe Leu Leu 395 Ala Glu Glu Val Cys Arg Cys Val Arg Thr Ser Trp Lys Arg Pro Leu 410 Met Asn

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$^{\circ}400 \! imes \! ^{\circ}21$ qttegetgec tagtgatggt gatggtgat	g 60
Hataatggaa tgaacttgto tgtaaacato dag	93
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0.210 × 34 0.211 × 22 0.212 × DMA 0.213 · Homo sapiens 400 · 34 caaacatgca ggtaagagat co	22
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ctombaaagt gotgggatta caggogtgag coacegtgto egaccaacet taagacaaa	C 180
aactactgca tgattgtttt tggagacctt ttttttattc aaataaattt ttgccagca	t 240
tttotgacto aaagtatago agcaggaaga taacactttt gtgagaaaaa agtttgaat	a 300
cagettactg etgtatttaa atgaaacagt agttaatatg atattaatat attttggat	a 360
tattttgagt ttgttgattt todagtette accegetget aggeetgtgg gtgttggaa	ia 420
tgmotgtgtt totoaatttt gtttgootat tagaatootg atgtooaago ottaotooa	ag 480
ttagaccagt taagccagaa aggcagaagg tgtactcaag catctgtttt ttcaaaatc	et 540

cettttgtga tgccaagtgc aatcaaagtt tagaatcatt gtaatagcaa atggttgaat 600 ggaaacteca cettetatte aaateetace eeagtetgee ettagetgtt etetttteae 660 agatotatoa atgiotgaag ataaotatgg caggotgato aaatatgoat agagoaggaa 720 gabagbaaga gagtgataba otgabbatgt tobaaatbab aaaabatbtb aabaggbtag 780 atcatggaco gagtotgatg ggatggaatt toataaagat acataaaaaa goatottgga 84) tadagtaaas ttaadtodad aaatadaggg gaatttagad gtgadtaagt agdagtadat 900 atgaaaaatt attgaggaat tttgttgact ttaagggtag tgtgagtcaa cactgtgatt 960 tggctgccag aaaataaact caatccaagg ctgtatcaac aaaggcatac tgtccattct 1020 geatgeteat tacageacta agtacegage catgttetea acegeataet teatgaacat 1080 ggaaagctaa cagtatggtt aaggggggaa actggaactg tcatcttggg gaataaaagg 1140 gatatttagc caggagtaaa gttagcttag ggagaccatg ataaatattt tcaaaatatt 1200 tgaaggactc agttgtggaa gtgagattag atttattgtg taaaactcca ggagtcaaaa 1260 gcaatagaga gatagaagga aatgetttte agcagtgttg eteateaata aagggagtga 1320 acagocadad agaatggaag gttoodtgtd otttgagata tttaagdott daagtaaatt 1380 atgggtgagg agtttcaaat ctagagttga accagataag aaagtctctt cttccggtaa 1440 gatattatgg acctatasca tetgtgtact taaaagtaga ttgggagtga aaggcagact 1900 tttgatgttd tgtadadtgt tgaaadddt tagdgtggtd dtdtgtaadd tgdtdadddi 1960 geoccaagga ggeagetage caatgecade ageocaaegg aaaccecagt getttteeaa 1620 tggggaaatg cagtcacttt tetttggatg ctacacatee tttetggaat atgteteaca 1680 cacatototo titatoacco cottittoaa giaaaccaao tiotigoaga agoigacaat 1740 gtgtetettt aeteteeaeg aagattetgg eeettetett eacetgteag aagtttagga 1800 ttocaaaggg atcattagca tocatoccaa cagootgoac tgcatoctga gaactgoggt 1860 tottggatoa toaggoaact ttoaactada dagaddaagg gagagagggg addddtddga 1920 ggtoccatag ggttototga catagtgatg acctttttoc aaactttgag cagggogotg 1980 ggggccaggc gtgcgggagg gaggacaaga actcgggagt ggccgaggat aaagcggggg 2040 otocotocac occaeggige coagittete ecogotycae giggicoagg giggicoat [100] cacetetada geoggiodeg ecaaeegeed geoeegggae igaaeitgee eeiceggeeg (1160) coegeteece geaggggaca ggggegggga gggagagate cagagggggg etgggggagg 2220 tggggccgcc ggggaggagg cgagggaaac ggggagctcc agggagacgg cttccgaggg 1280 agagtgagag gggagggcag cccgggctcg gcacgctccc tccctcggcc gctttctctc 2340 acataagogo aggoagaggg ogogtoagto atgodotgoo ootgogoogg oogoogoogo 2400 egeogeoget cagecoggeg egetetggag gateotgege egeggegete cogggeeceg 2460

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 Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
 Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
 Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
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 Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
                                  105
 Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
                            120
  Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
                         135
  Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
                      150
  Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
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  Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
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25

- 27 -

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- 28 -

<400> 55

Met Pro Val Met Arg Leu Phe Pro Cys Phe Leu Gln Leu Leu Ala Gly 10 Leu Ala Leu Pro Ala Val Pro Pro Gln Gln Trp Ala Leu Ser Ala Gly Asn Gly Ser Ser Glu Val Glu Val Val Pro Phe Gln Glu Val Trp Gly Arg Ser Tyr Cys Arg Ala Leu Glu Arg Leu Val Asp Val Val Ser Glu Tyr Pro Ser Glu Val Glu His Met Phe Ser Pro Ser Cys Val Ser Leu Leu Arg Cys Thr Gly Cys Cys Gly Asp Glu Asn Leu His Cys Val Pro Val Glu Thr Ala Asn Val Thr Met Gln Leu Leu Lys Ile Arg Ser Gly 100 Asp Arg Pro Ser Tyr Val Glu Leu Thr Phe Ser Gln His Val Arg Cys 120 Glu Cys Arg Pro Leu Arg Glu Lys Met Lys Pro Glu Arg Cys Gly Asp 135 Ala Val Pro Arg Arg 145 <210> 56 <211> 191 <212> PRT <213> Homo sapiens <220> <223> VEGF165 precursor Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu 55 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 105 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys 115

Glu Cys Arg Pro Dys Dys Asp Arg Ala Arg Gln Glu Asn Pro Cys Gly 135 130 Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln 170 Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg 185 3210× 57 1211> 188 :112> PRT <213> Homo sapiens <220> <223> VEGF-B167 Met Ser Pro Leu Leu Arg Arg Leu Leu Leu Ala Ala Leu Leu Gln Leu Ala Pro Ala Gln Ala Pro Val Ser Gln Pro Asp Ala Pro Gly His Gln Arg Lys Val Val Ser Trp Ile Asp Val Tyr Thr Arg Ala Thr Cys Gln Fro Arg Glu Val Val Pro Leu Thr Val Glu Leu Met Gl; Thr Val Ala Lys Gln Leu Val Pro Ser Cys Val Thr Val Gln Arg Cys Gly Gly Cys Cys Pro Asp Asp Gly Leu Glu Cys Val Pro Thr Gly Gln His Gln Val Arg Met Gln Ile Leu Met Ile Arg Tyr Pro Ser Ser Gln Leu Gly 105 Glu Met Ser Leu Glu Glu His Ser Gln Cys Glu Cys Arg Pro Lys Lys Lys Asp Ser Ala Val Lys Pro Asp Ser Pro Arg Pro Leu Cys Pro Arg 135 Cys Thr Gln His His Gln Arg Pro Asp Pro Arg Thr Cys Arg Cys Arg 150 Cys Arg Arg Ser Phe Leu Arg Cys Gln Gly Arg Gly Leu Glu Leu 170 Asn Pro Asp Thr Cys Arg Cys Arg Lys Leu Arg Arg 185 180 c210: 58 :211: 419 <212> PPT <213> Artificial Sequence

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<223 Description of Artificial Sequence: VEGF C delta Cys156 mutant <223> At position 156, "Xaa" can be anything other than cysteine or can be nothing Met His Leu Leu Gly Phe Phe Ser Val Ala Cys Ser Leu Leu Ala Ala Ala Leu Leu Pro Gly Pro Arg Glu Ala Pro Ala Ala Ala Ala Phe Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu Ala Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys Met Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu Gln Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Xaa Val Ser Val Tyr 150 145 Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser 200 Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile 215 Ile Arg Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn Lys Thr Cys Pro Thr Asn Tyr Met Trp Asn Asn His Ile Cys Arg Cys Leu Ala Gln Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser 265 Thr Asp Gly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu

Glu Thi Cys Gln Cys Val Cys Arg Ala Gly Leu Arg Pro Ala Ser Cys Gly Pro His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys Asn Lys Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu Asn Thr Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro Leu Asn Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys Cys Leu Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr Arg Arg Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser Tyr Ser Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro Gln Met Ser <210> 59 <211> 160 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: VEGF-C delta N delta CHis Met His Leu Leu Gly Phe Phe Ser Val Ala Cys Ser Leu Leu Ala Ala Ala Leu Leu Pro Gly Pro Arg Glu Ala Pro Ala Ala Ala Ala Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys Asn 85 Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro Val

Thr lie Ser Phe Ala Ash His Thr Ser Cys Arg Cys Met Ser Lys Leu 130 135

Asp Val Tyr Arg Glm Val His Ser Ile Ile His His His His His His 160